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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,630	01/25/2002	Ronald M. Burch	200.1079CON5	3300

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EXAMINER	
GROSS, CHRISTOPHER M	
ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/057,630	BURCH ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER M. GROSS	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38 and 47-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 47-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/5/2010;4/22/2010;11/5/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Responsive to communications entered 3/8/2010; 11/5/2008. Claims 38,47-76 are pending. Claims 38,47-76 are under consideration.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/8/2010 has been entered.

Election/Restrictions

Newly submitted/amended claims 63-67, 71, 73, 75, 76 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons.

The 11/5/2010 remarks allege that the 6/26/2008 elected species of arthritic pain reads on claims 63, 71 and 73 in view of evidence provided by Koch et al (1997 Textbook of Internal Medicine, third edition, Lippincott–Raven pp 1091-1093 – IDS entry 11/5/2010) showing the initial diagnosis of monoarticular arthritis is whether it is inflammatory or noninflammatory.

This is not deemed persuasive for the following reasons. First, the literal definition of "arthritis," Greek *arthro-*, joint + *-itis*, inflammation. Second, claim 67, which further limits claim 63 is drawn to, toothaches, sprains and strains, bursitis, common colds and gout, each of which are associated with swelling (inflammation). In fact, said gout, is explicitly indicated as inflammatory monoarticular arthritic pain in accordance with Koch et al figure 170-1.

Nevertheless, in the spirit of compact prosecution, claims 63-67, 71, 73, 75, 76 are retained for examination.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 or 119 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the prior application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Prods., Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994) [taken from MPEP 201.01]

The instant application, filed 1/25/2002 claims priority as a CON of application 09/154,354 09/17/1998 (now PAT 6,552,031) which claims benefit of provisional application 60/059,195 filed 09/17/1997.

It is noted, however, the following limitations are not disclosed in the earlier applications.

1. A method of effectively treating pain in humans, comprising orally administering to a human patient a therapeutically effective amount of nimesulide together with a dose of oxycodone (i.e. two separate pills), as set forth in claim 38.

2. Any ratio of oxycodone to nimesulide , as set forth in claims 38,54 and 64, much less 10:1, as set forth in amended claims 47, 64, 74.

3. an oxycodone salt in sustained release form as set forth claims 50, 54, 60, 61, 65; as well as the materials therefor of claim 56; and tablet dimensions set forth in claims 58-59.

4. a sustained release carrier incorporated in a oxycodone matrix of claim 61.

If applicant believes this assessment is in error, applicant is to indicate as to page and line where support for each of the above limitations may be found in the earlier applications.

See also 35 USC 112 first paragraph rejection below items 1-3 constituting new matter.

As none of the above limitations are disclosed in the earlier applications, 1/25/2002 is the date for the purposes of prior art concerning claims 38,47-76.

Discussion

With the exception of items 3-4, above, to which applicant has not pointed to support, applicant's 3/8/2010 amendments and arguments have largely addressed the priority concerns raised in the last office action. However, the claims as currently amended introduce further limitations which are not disclosed in the earlier application(s) as follows.

Page 7 of the 3/24/2010 remarks asserts that support for the amendments to claim 38 may be found on p 15 lines 14-23 taken with p 12 lines 11-16 of the provisional application. It is noted however, in context, the passage on p 15 recites a "therapeutically effective amount of [] COX-2 inhibitor and opioid analgesic **combination**" (Emphasis added), as opposed to taking two separate pills, one oxycodone, one nimesulide, as set forth in amended claim 38. Additionally the passage on p 12 of the provisional application refers to ratios of oxycodone to nimesulide limited to the range (0.005-48) shown in table I, as opposed to any ratio, as set forth in claims 38, 54 and 63. Furthermore, while it is acknowledged that the 3/24/2010 remarks allege that support for said 10:1 (item 2) may be found on p 13 line 7 of the provisional, drawn to a certain preferred (singular) embodiment of oxycodone 40 mg plus 4 mg nimesulide, this does not provide support for the more general 10:1 combination (e.g. 4 mg plus 0.4 mg; 400 mmol plus 40 mmol, etc; see also 35 USC 112 second paragraph rejection below) as set forth in amended claims of claims 47, 64 and 74.

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Maintained Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 38, 47-48, 50-53, 49 plus 54-68 plus 69-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Baker et al** (US patent 4,569,937) in view of **Swingle et al.** (Drugs Exptl. Clin. Res. Vol. X(8-9) (1984) pages 587-597) **and/or Rabasseda** (Drugs of Today Vol. 32, No. 5 (1996) pages 365-384) and further in view of **Oshlack et al**. US Pat. No. 5,472,712 (referred to as **'712**) or **Oshlack et al.** US Pat. No. 6,294,195 (referred to as **'195**) as evidenced by Beaver (1984 Combination Analgesics. The American Journal of Medicine pp 38-53) and Beaver II (1992 Evaluation and Treatment of Chronic Pain Ch 29 Nonsteroidal antiinflammatory analgesics and their combinations with opioids) for the reasons set forth in the office actions mailed beginning 1/19/2005.

Please note the above rejection has been modified from the prior version(s) to more clearly address applicant's amended and/or new claims as follows.

With regard to amended claims 47, 64 and new claim 74, Oshlack '195 teach in column 6 line 50, 400 mg oxycodone whereas Swingle et al teach in figure 6, nimesulide dosages ca. 4 mg/kg body weight, thus for a 10 kg child, 40 mg. Accordingly, the combined teachings of Oshlack et al and Swingle et al suggest a 10:1 ratio (interpreted as mass; see 35 USC 112 second paragraph rejection below).

With regard to amended claims 49-50, 56, 60 Oshlack et al '195 teach from column 6 line 64 to column 9 line 58, combinations of said oxycodone opioid with non-steroidal anti-inflammatory drugs (NSAIDs; the NSAID/COX-2 inhibitor nimesulide is provided by Rabasseda or Swingle et al) including a single dosage form having sustained release carrier materials. The same passage teaches the NSAID in

immediate release form per claim 54 (i), the sustained release of opioid per claim 54 (ii) and plasticizers as an additional excipient per claim 54 (iii) as well as the admixture of excipients per claim 63 lines 2-3. Alternatively, the passage teaches incorporating the NSAID in a matrix with the opioid per (elected species) as well as sustained release coatings, each per claims 61 and/or 69. The passage also teaches ethylcellulose (an alkylcellulose; elected species) as a sustained release carrier per claim 56.

With regard to amended claim 55, Oshlack '195 teach 12 hour dosing (2 times per day) in column 4 line 14.

Oshlack et al '195 teach in column 4 line 38, dosing every 24 hours (once-daily), per amended claim 62 and new claims 72 and 76.

With regard to new claims 70 and 75, Swingle et al teach in figure 3, effective nimesulide dosages as low as ca. 1 mg/kg body weight, thus for a 4 kg child, 4 mg.

With regard to pain without inflammation, as set forth in amended claim 63 and 71, 73 as well as 67, Rabasseda teaches non-inflammatory (e.g. surgical) pain on p 373 right column first paragraph.

Response to Arguments

The 3/8/2010 remarks argue (i) the claimed subject matter is not obvious; (ii) not all elements are taught.

Applicant's arguments have been fully considered but they are not deemed persuasive for the following reasons.

(i) Specifically, in regard to the Beaver articles mentioned in the last office action, p 11 of the remarks notes Beaver indicates that an analgesic combination is only called

for, if analgesia is not affected by an NSAID alone and there is nothing in the cited references to say that nimesulide will not provide adequate analgesia alone.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., inadequate analgesia provided by nimesulide alone) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

(ii) (a) With regard to independent claim 54, p 12 second paragraph of the remarks assert page 6 the last office action does not point to a teaching of a COX-2 inhibitor in an immediate release form.

In this vein, as mentioned above, applicant's attention is respectfully invited in particular to column 7 lines 8-28 of Oshlack '195, which explicitly recites an NSAID in immediate release form; the NSAID/COX-2 inhibitor being nimesulide is provided by Rabasseda or Swingle et al.

(ii) (b) With regard to claims 47 and 64, p 12 last paragraph of the remarks assert Baker et al teach narcotics analgesics to the NSAID in the range 1:1 to 1:800 the inverse (reciprocal) of what is claimed (10:1).

Here, as detailed above, the combined teachings of Oshlack et al and Swingle et al suggest a 10:1 ratio (interpreted as mass; see 35 USC 112 second paragraph rejection below).

(ii) (c) With regard to claim 62, p 12 last paragraph of the remarks assert none of Rabasseda nor Swingle et teach once-daily dosing.

In this vein, it is noted that claim 54, from which claim 62 depends from is drawn to an oral dosage form consisting of nimesulide and oxycodone. As detailed above, once-a-day dosings of oxycodone and combinations thereof is provided by Oshlack '195.

With regard to both points (ii) (a-c) above, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

35 USC § 112

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38,47-68 plus 69-76 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection concerns new matter.

Claim 38 has been amended to be drawn to an effective amount of nimesulide and oxycodone as two separate pills.

Each of independent claims 38,54 and 64 are each drawn to any ratio of oxycodone to nimesulide.

Claims 47, 64, 74.are each drawn to a "10:1" ratio of oxycodone to nimesulide.

Claims 50, 54, 60 and 61 are each drawn to an oxycodone salt in a sustained release form with materials therefor in claim 56 and the tablet dimensions thereof in claims 58-59.

Neither the specification as originally filed nor the priority document provided implicit or explicit support for the above limitations.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the disclosure. See MPEP 714.02, paragraph 5, last sentence and also MPEP 2163.06 I.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP

2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure*.

***

Please note that the above rejection has been modified from the original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Discussion

Page 7 of the 3/24/2010 remarks asserts that support for the amendments to claim 38 may be found on p 9 lines 13-15 taken with p 19 lines 15-20 of the original specification. It is noted however, in context, the passage on p 9 recites a "therapeutically effective amount of a COX-2 inhibitor together with a dose of opioid analgesic, such that the **combination provides an analgesic effect which is at least about 5**" (Emphasis added), as opposed to taking two separate pills, one oxycodone, one nimesulide and further without regard to analgesic effect, as set forth in amended claim 38. Additionally the passage on p 9 of the original specification refers to ratios of oxycodone to nimesulide limited to the range 0.0001-1 shown in table I, as opposed to any ratio, as set forth in claims 38, 54 and 64, much less the reciprocal 10:1 ratio of claims 47, 64 and 74. Furthermore, while it is acknowledged that the 3/24/2010 remarks allege that support for said 10:1 may be found on p 20 lines 22-23 of the provisional, drawn to a certain preferred (singular) embodiment of oxycodone 40 mg plus 4 mg

nimesulide, outside said 0.0001-1, this does not provide support for the more general 10:1 combination (e.g. 4 mg plus 0.4 mg; 400 mmol plus 40 mmol, etc.) set forth in claims 47, 64 and 74.

New Claim Rejection - 35 USC § 112

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47,64 and 74 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "10:1" in each of claims 47,64 and 74 is a relative term which renders the claim indefinite. The term "10:1" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In particular, due to the lack of units, it is not clear if the ratio is with regard to mass, moles, volume, etc, rendering the meets and bounds of the claims unascertainable.

In accordance with MPEP 2173.02: If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. See *Morton Int 'l, Inc. v. Cardinal Chem.* Co., 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER M. GROSS whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JoAnne Hama can be reached at 571 272-2911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christopher M Gross/
Examiner, Art Unit 1639

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